Sleep Medicine 15 (2014) 1062–1067

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

# Poor sleep quality measured by polysomnography in non-obese asthmatic children with or without moderate to severe obstructive sleep apnea

Yu-Kuei Teng [a,b], Li-Chi Chiang [c], Ko-Huang Lue [d,e], Shen-Wen Chang [f], Lee Wang [g], Shu-Ping Lee [h], Hua Ting [f,i,1], Shin-Da Lee [a,j,k,1,*]

[a] Graduate Institute of clinical medical science, China Medical University, Taichung, Taiwan
[b] School of Nursing, China Medical University, Taichung, Taiwan
[c] School of Nursing, National Defense Medical Center, Taiwan
[d] Department of Pediatrics, Chung Shan Medical University Hospital Taichung, Taiwan
[e] School of Medicine, Chung Shan Medical University Taichung, Taiwan
[f] Center of Sleep Medicine, Chung-Shan Medical University Hospital, Chung-Shan Medical University, Taichung, Taiwan
[g] Department of Public Health, Chung-Shan Medical University, Taichung, Taiwan
[h] Department of Foreign Languages and Literature, Asia University, Taichung, Taiwan
[i] Department of Physical Medicine and Rehabilitation, Chung-Shan Medical University Hospital, Chung-Shan Medical University, Taichung, Taiwan
[j] Department of Physical Therapy, Graduate Institute of Rehabilitation Science, China Medical University, Taichung, Taiwan
[k] Department of Healthcare Administration, Asia University, Taichung, Taiwan

ARTICLE INFO

*Article history:*
Received 19 November 2013
Received in revised form 18 March 2014
Accepted 15 April 2014
Available online 6 June 2014

*Keywords:*
Asthma
Child
Obstructive sleep apnea
Polysomnography
Sleep

ABSTRACT

*Background:* The co-effect of asthma and obstructive sleep apnea (OSA) on sleep quality among children remained unclear.
*Objective:* To compare sleep quality and emotional/behavioral problems among asthmatic and non-asthmatic children with or without moderate to severe obstructive sleep apnea.
*Method:* An AHI-range-matched BMI-range-matched cross-sectional design was used to examine polysomnographic evaluation and emotional/behavioral problems in 102 non-obese children aged between 6 and 12 years old, categorized as with or without asthma and sleep disordered breathing.
*Results:* Asthmatic children in AHI ≤ 5/h group revealed a significantly longer sleep latency, a greater leg movement index (LMI), and a lower ratio of slow wave sleep compared with non-asthmatic AHI ≤ 5/h group. Compared with non-asthmatic AHI > 5/h group, asthmatic children displayed a higher ratio of REM sleep, sleep stage 1 and 2, a lower ratio of slow wave sleep, as well as a greater respiratory arousal index and LMI. There was no significant difference in emotional/behavior problems among groups.
*Conclusion:* Sleep disturbance exists in asthmatic children with or without moderate to severe obstructive sleep apnea. Non-obese asthmatic children had less slow wave sleep compared with non-asthmatic children. We might recommend that sleep quality could be noticed and evaluated in children with asthma.



## 1. Introduction

Asthma, which is an inflammatory and hyper-responsive condition of the airways, is one of the most common chronic illnesses in children. The under-reporting of nocturnal asthma symptoms was found in previous studies [1,2]. Children with nocturnal symptoms had poor forced expiratory volume in first second, lower daytime activities, and worse health perceptions than those without nocturnal symptoms [2].

Obstructive sleep apnea (OSA) is a disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction [3]. Children with OSA have more arousals from sleep than normal children [4], but the proportion of the different stages of sleep have not been investigated compared to adults [5,6]. Obesity is a risk factor and a confounding factor of pediatric sleep apnea and asthma [7].

Nocturnal asthma symptoms might contribute to disrupted sleep, daytime tiredness, daytime sleepiness, and reduced alertness [8]. In a study by Fitzpatrick et al., over 80% of the asthmatic subjects woke at night with wheezing, and subjects with asthma had a lower sleep time than subjects without asthma [9]. The polysomnography,

* Corresponding author at: Shin-Da Lee, PhD, No. 91, Hsueh-Shih Road, Taichung 404, Taiwan. Tel.: 886 4 22053366*7300; fax: 886 4 22065051.
*E-mail address:* shinda@mail.cmu.edu.tw (S.-D. Lee).
[1] Shin-Da Lee and Hua Ting share equal contribution.

http://dx.doi.org/10.1016/j.sleep.2014.04.017
1389-9457/

gold standard for evaluation of sleep [10], data in asthmatic children were found to include longer sleep latency, greater respiratory arousal index, and longer total sleep time than those in non-asthmatic children [11]. AHI was significantly higher in subjects with poorly controlled asthma and poor sleep efficiency [12]. Until now the iso-effect, or co-effect, of asthma and OSA on sleep quality evaluated by PSG among non-obese children remains unclear.

Behavioral problems and asthma symptoms demonstrate a statistically significant association [13]. Research has been reported in which children's internalizing symptoms ranked by parents, such as depression, somatic complaints, and social withdrawal were related to the severity of their asthma [14]. A recent study has shown that behavioral problems are associated with poor sleep in children with asthma [15]. Asthma severity may be considered as a possible risk factor for behavioral problems. However, behavior problems have not been demonstrated among non-obese children with mild asthma and with OSA.

Only a few studies have used objective measurement of PSG to report sleep quality among children with asthma [11,16,17]. The relationship of OSA and asthma on sleep quality among non-obese children has not been investigated in studies. Therefore, the purposes of the present study were to compare sleep quality and quantity as measured by PSG, and to compare behavioral problems in non-obese asthmatic children, with or without moderate to severe obstructive sleep apnea. We hypothesized that asthmatic children, with or without moderate to severe obstructive sleep apnea, will exhibit poorer sleep quality and a poorer grade in behavioral problems than non-obese non-asthmatic children, with or without moderate to severe obstructive sleep apnea.

## 2. Methods

### 2.1. Subjects

A total of 102 non-obese children aged between 6 and 12 years old were recruited from several elementary schools in this study. The study was announced by the school nurse. Subjects were recruited by purposive sampling, and all visited pediatric clinics to check their asthma status and evaluate sleep disturbance. Asthmatic children met the standard criteria for a diagnosis of asthma, which included a physician's diagnosis based on the criteria of asthma symptoms and medical history such as coughing, episodic breathlessness, wheezing and chest tightness as well as a methacholine bronchoprovocation test PC20 of 8 mg/ml or less [18]. The cutoff point for the apnea–hypopnea index was based on children criteria [19]. Exclusion criteria included respiratory diseases other than asthma, pain or discomfort conditions, obesity (body mass index above 95th percentile) [20], acute asthma exacerbations, serious physical or psychiatric disorders, and condition of AHI range cannot be matched. For evaluating asthma effect during sleep, AHI-range-matched weight-range-matched non-asthmatic children whose AHI ≤ 5/h and AHI > 5/h were recruited and analyzed as control groups. Children were categorized into four groups, which were non-asthmatic children with AHI ≤ 5/h, asthmatic children with AHI ≤ 5/h, non-asthmatic children with AHI > 5/h, and asthmatic children with AHI > 5/h by diagnosis of asthma and sleep disordered breathing.

### 2.2. Polysomnography (PSG)

The sleep quality of all children was examined by PSG. Recorded parameters included four electroencephalogram channels, two electrooculogram channels, one chin and two leg electromyogram channels, nasal flow cannula, oronasal airflow thermistor, end-tidal $CO_2$ cannula, chest and abdominal respiratory Piezo crystal belts, electrocardiogram, and oxygen saturation. Sleep stages and obstructive apnoeic episodes were scored according to standard criteria [10].

An obstructive apnoeic episode was defined by cessation of airflow for more than two respiratory cycles in the presence of respiratory effort. Hypopnea was defined by a 50% reduction in respiratory airflow accompanied by a decrease of >4% in oxyhemoglobin saturation and/or an arousal. AHI was defined by the number of obstructive apnea and hypopnea episodes per sleeping hour. In addition, physiologic parameters were recorded: the total sleep time in minutes (TST), the sleep efficiency, the sleep latency, rapid eye movement (REM) latency, the percentage of time in REM sleep, the percentage of time in non-rapid eye movement (NREM) sleep (divided into NREM stage 1 and 2 combined and NREM stage 3 and 4 combined), the lowest oxygen saturation over 10 s (Nadir $SpO_2$ over 10 s), and the duration of saturation below 90% (Time $SpO_2 < 90\%$). An arousal index, with or without a respiratory event, was defined by the number of arousals or shifts in the sleep stage to a "wake" pattern lasting more than 3 s but less than 15 s divided by the total sleep. Leg movements were defined as events of tibialis anterior muscle activity with a duration between 0.5–5 s and with an amplitude of at least 25% of the events recorded that corresponded to no activity at background level, with each movement being separated from another by at least 1 s. Periodic leg movements were defined as events of tibialis anterior muscle movement occurring in a series of four or more events, with inter-movement intervals between 5 and 90 s. Leg movements related to respiratory events were defined as a respiratory event which must follow a leg movement with a delay of less than 3 seconds [21]. The leg movement index (LMI), periodic leg movement index (PLMI), and leg movement index related respiratory event (RRLMI) were derived by dividing the number of LM, PLM and RRLM by the sleep time (in hours).

### 2.3. Child Behavior Checklist (CBCL)

The CBCL was designed to assess emotional and behavioral problems in children of 4–18 years of age, by parent or care-giver ratings. The CBCL is derived from the 113 emotional and behavioral items and includes nine behavioral aspects: withdrawal, anxiety/depression, somatic complaints, social problems, thought problems, attention problems, delinquent behaviors, aggressive behaviors and one other. Parents were asked to rate their children's problems on a 3-point scale (0: not true; 1: sometimes true; 2: very true/often true) during the previous 6 months. The three scales of this questionnaire are expressed in scores for: anxiety/depression, withdrawal, and somatic complaints for internalization; aggressive and delinquent behavior for externalization; and global score. Scores were transformed into age- and gender-standardized T-scores. Higher T-scores depict expanded behavioral problems. The reliability and validity of the CBCL were determined to be satisfactory for Taiwanese adolescents [22].

### 2.4. Procedure

A cross-sectional study was used to investigate sleep quality based on asthma disease and respiratory disturbance in children aged 6–12 years old. The effective size of the pilot study was estimated by a mean difference of 9 min and standard deviation of 15. The sample size calculation was performed to detect a 0.5 standardized mean difference in sleep latency between the asthmatic group and non-asthmatic group with a power of 80% and a type one error of 5%. We enrolled 51 subjects in both the asthmatic children group and non-asthmatic children group. The study was approved by the Institutional Review Board prior to commencement. After being provided with a description of the procedures and purposes of the study, informed consent was obtained from all parents or guardians of the

**Table 1**
Demographic and pulmonary function data.

| | AHI ≤5 | | AHI >5 | | *p*-value | | |
|---|---|---|---|---|---|---|---|
| | Non-asthmatic children[a] ($n = 23$) | Asthmatic children[b] ($n = 23$) | Non-asthmatic children[c] ($n = 28$) | Asthmatic children[d] ($n = 28$) | a vs. b | c vs. d | a vs. d |
| Gender (% male) | 52.2 | 39.1 | 64.3 | 60.7 | 0.55 | 10.00 | 0.10 |
| AHI (events/h TST) | 2.64 ± 1.25 | 2.92 ± 0.97 | 10.14 ± 5.30 | 10.23 ± 4.97 | 0.41 | 0.95 | <0.001 |
| Snore index (events/h TST) | 191.10 ± 155.28 | 210.90 ± 268.98 | 229.82 ± 221.78 | 316.33 ± 237.63 | 0.99 | 0.64 | 0.03 |
| Age (years) | 9.35 ± 1.56 | 9.57 ± 1.20 | 9.71 ± 1.01 | 9.21 ± 1.37 | 0.60 | 0.13 | 0.74 |
| Neck circumference (cm) | 29.22 ± 2.24 | 28.61 ± 2.31 | 28.66 ± 1.87 | 29.13 ± 3.14 | 0.37 | 0.51 | 0.91 |
| Waist circumference (cm) | 66.13 ± 8.88 | 64.72 ± 11.41 | 64.07 ± 7.44 | 64.54 ± 8.69 | 0.64 | 0.83 | 0.53 |
| Hip circumference (cm) | 77.59 ± 8.55 | 76.37 ± 11.56 | 74.88 ± 7.34 | 75.32 ± 9.07 | 0.69 | 0.84 | 0.36 |
| BMI (kg/m$^2$) | 17.93 ± 3.24 | 18.18 ± 3.78 | 17.56 ± 2.48 | 18.14 ± 3.20 | 0.82 | 0.45 | 0.82 |
| BMI *z*-score | 0.30 ± 0.86 | 0.29 ± 1.10 | 0.29 ± 0.62 | 0.30 ± 0.90 | 0.97 | 0.96 | 1.00 |
| $FEV_1$ (% predicted) | 105 ± 9 | 87 ± 9 | 102 ± 8 | 87 ± 7 | <0.001 | <0.001 | <0.001 |
| FVC (% predicted) | 92 ± 10 | 81 ± 8 | 89 ± 10 | 83 ± 6 | <0.001 | 0.009 | <0.001 |
| $FEV_1$/FVC (% predicted) | 100 ± 5 | 93 ± 7 | 101 ± 6 | 87 ± 11 | <0.001 | <0.001 | <0.001 |
| $FEF_{25–75}$ (% predicted) | 132 ± 16 | 98 ± 27 | 123 ± 10 | 87 ± 19 | <0.001 | <0.001 | <0.001 |

AHI, apnea–hypopnea index; TST, total sleep time; BMI, body mass index; $FEV_1$, forced expiratory volume (during first second); FVC, forced vital capacity; $FEF_{25–75}$, forced expiratory flow (25–75% of VC).
For quantitative variables, data are presented as mean ± standard deviation (SD) for normally distributed data. For categorical variables, data are presented as count percentage; $p < 0.05$ significant differences from relative control group.
[a] Non-asthmatic children in AHI ≤ 5 group.
[b] Asthmatic children in AHI ≤ 5 group.
[c] Non-asthmatic children in AHI > 5 group.
[d] Asthmatic children in AHI > 5 group.

participating children. After enrollment, children received an asthma diagnostic evaluation and overnight sleep evaluation. As the children were undergoing their asthma evaluation, the parents were asked to complete a questionnaire which included questions concerned with emotional and behavioral problems. The overnight sleep evaluation occurred within 2 weeks at the sleep laboratory at Chung Shing Hospital. The aim of this study was to compare sleep quality in children who were either asthmatic or non-asthmatic, with or without moderate to severe obstructive sleep apnea [apnea–hypopnea index (AHI) > 5 events/h during sleep or not]. The outcome measures included sleep quality and parent-reported emotional and behavioral problems.

### 2.5. Data analysis

SPSS for Windows (version 17.0) was used to calculate descriptive and inferential statistics. Results were presented as numbers and percentages for categorical data and were expressed as mean and standard deviation for continuous data. Demographic data, polysomnographic data and behavioral problems were using ANOVA with preplanned contrast comparison analysis to compare with AHI-range-matched BMI-range-matched non-asthmatic non-obese group. In addition, we also compare asthmatic children with AHI > 5/h to non-asthmatic children with AHI ≤ 5/h to clarify asthma plus OSA effect. Chi-square was performed to analyze asthma symptoms among asthmatic children. Statistical significance was set as $\alpha < 0.05$.

## 3. Results

### 3.1. Demographic and pulmonary function data

Of the total subjects, 56 boys and 46 girls completed the PSG in this study. Children were categorized into four groups by diagnosis of asthma and sleep disordered breathing. Forty-six children were in AHI ≤ 5 group, i.e., 23 children with asthma and 23 children without asthma. Fifty-six children were in AH I> 5 group, i.e., 28 children with asthma and 28 children without asthma. The homogeneity test showed that the demographic data were homogeneous between the asthmatic children and non-asthmatic children within the two respiratory disturbance groups, except the items of pulmonary function data, AHI and snore index (Table 1). Age, neck circumference, waist circumference, hip circumference, BMI, BMI *z*-score, and gender distribution were similar among comparison groups. The percentage of allergic rhinitis in asthmatic children is greater than in non-asthmatic children by parental reporting (3.9% vs. 66.7%). The pulmonary function data of asthmatic children were poorer than those of non-asthmatic children. No significant differences were showed on asthma symptoms between asthmatic children with AHI ≤ 5/h and asthmatic children with AHI ≤ 5/h (Table 2).

### 3.2. Comparison of emotional and behavioral problems

As seen in Table 3, comparison between asthmatic children and non-asthmatic children with AHI > 5/h showed no significant ($p > 0.05$) changes in CBCL scores. Mean parent-reported emotional and behavioral symptoms scores were not statistically significant ($p > 0.05$) between asthmatic children and non-asthmatic

**Table 2**
Asthma symptoms among asthmatic children.

| | AHI ≤5 | | AHI >5 | | *p*-value |
|---|---|---|---|---|---|
| | No. ($N = 23$) | % | No. ($N = 28$) | % | |
| Chest tightness during sleep | | | | | 0.76 |
| No symptoms | 13 | 56.5 | 17 | 60.7 | |
| Mild to moderate symptoms | 10 | 43.5 | 11 | 39.3 | |
| Cough | | | | | 0.72 |
| No symptoms | 4 | 17.4 | 6 | 21.4 | |
| Mild to moderate symptoms | 19 | 82.6 | 22 | 78.6 | |
| Wheezing | | | | | 0.88 |
| No symptoms | 12 | 52.2 | 14 | 50.0 | |
| Mild to moderate symptoms | 11 | 47.8 | 14 | 50.0 | |
| Exercise-induced shortness of breath | | | | | 0.83 |
| No symptoms | 10 | 43.5 | 13 | 46.4 | |
| Mild to moderate symptoms | 13 | 56.5 | 15 | 53.6 | |

AHI, apnea–hypopnea index.
No difference in asthma symptoms among asthmatic children between AHI ≤5 and AHI >5.

**Table 3**
Parent-reported emotional and behavioral problems in Child Behavior Checklist.

| | AHI ≤5 | | AHI >5 | | *p*-value | | |
|---|---|---|---|---|---|---|---|
| | Non-asthmatic children[a] ($n = 23$) | Asthmatic children[b] ($n = 23$) | Non-asthmatic children[c] ($n = 28$) | Asthmatic children[d] ($n = 28$) | a vs. b | c vs. d | a vs. d |
| Internalization behavior problems | 63.00 ± 3.46 | 62.29 ± 8.81 | 59.80 ± 10.09 | 61.20 ± 8.09 | 0.72 | 0.57 | 0.29 |
| Externalizing behavior problems | 56.25 ± 4.79 | 55.00 ± 4.83 | 59.13 ± 5.46 | 56.73 ± 6.93 | 0.38 | 0.16 | 0.30 |
| Total behavior problems | 50.75 ± 3.30 | 49.50 ± 4.23 | 50.29 ± 6.53 | 50.21 ± 6.27 | 0.27 | 0.96 | 0.70 |

AHI, apnea–hypopnea index.
Data are presented as mean ± standard deviation (SD).
[a] Non-asthmatic children in AHI ≤ 5 group.
[b] Asthmatic children in AHI ≤ 5 group.
[c] Non-asthmatic children in AHI > 5 group.
[d] Asthmatic children in AHI > 5 group.

children with AHI ≤ 5/h. The emotional and behavioral symptoms scores were not statistically significant ($p > 0.05$) between non-asthmatic children with AHI ≤ 5/h and asthmatic children with AHI > 5/h.

### 3.3. Comparison of sleep quality

Table 4 summarizes the polysomnographic variables in sleep architecture among asthmatic children and non-asthmatic children without and with sleep apnea. Compared with non-asthmatic children in the AHI ≤ 5/h group, asthmatic children in the AHI ≤ 5/h group had significantly longer sleep latency (25.59 ± 20.73 vs. 10.63 ± 9.59 min, $p = 0.004$), a greater rate of LMI (5.12 ± 2.69 vs. 3.40 ± 2.93 n/h, $p = 0.04$), and a lower ratio of slow wave sleep (43.35 ± 13.16 vs. 52.59 ± 14.11%, $p = 0.03$) as well as asthmatic children in the in AHI > 5/h group had significantly higher ratio of sleep stage 1 and 2 (41.23 ± 12.57 vs. 32.78 ± 13.15%, $p = 0.02$), a greater rate of respiratory arousal index (5.14 ± 4.00 vs. 1.67 ± 2.25 n/h, $p < 0.001$), a greater rate of RRLMI (0.36 ± 0.48 vs. 0.03 ± 0.09 n/h, $p = 0.001$), and a lower ratio of slow wave sleep (41.38 ± 11.73 vs. 52.59 ± 14.11%, $p < 0.001$).

Compared with the non-asthmatic children in AHI > 5/h, asthmatic children exhibited a higher ratio of REM sleep (17.39 ± 5.22 vs. 13.43 ± 5.41 %, $p = 0.007$), sleep stage 1 and 2 (41.23 ± 12.57 vs. 29.18 ± 12.8 %, $p = 0.001$), and lower ratio of slow-wave sleep (41.38 ± 11.73 vs. 57.48 ± 11.41%, $p < 0.001$). Asthmatic children had a greater respiratory arousal index (5.14 ± 4.00 vs. 3.22 ± 2.94 n/h, $p = 0.04$), and LMI (4.84 ± 2.44 vs. 2.77 ± 3.40 n/h, $p = 0.01$) in comparison with non-asthmatic children in the AHI > 5/h group.

## 4. Discussion

Three major findings were found in this study. First, asthmatic children without moderate to severe obstructive sleep apnea had significantly longer sleep latency than AHI-range-matched BMI-range-matched non-asthmatic children. Second, asthmatic children without sleep apnea had less slow wave sleep compared with AHI-range-matched BMI-range-matched non-asthmatic children.

**Table 4**
Comparison of sleep quality parameters across AHI with/without asthma.

| | AHI ≤ 5 | | AHI > 5 | | *p*-value | | |
|---|---|---|---|---|---|---|---|
| | Non-asthmatic children[a] ($n = 23$) | Asthmatic children[b] ($n = 23$) | Non-asthmatic children[c] ($n = 28$) | Asthmatic children[d] ($n = 28$) | a vs. b | c vs. d | a vs. d |
| TST (min) | 320.30 ± 64.85 | 345.35 ± 45.40 | 325.32 ± 30.18 | 340.36 ± 41.03 | 0.14 | 0.12 | 0.20 |
| Sleep efficiency (%) | 90.13 ± 6.65 | 86.87 ± 7.31 | 89.57 ± 7.22 | 90.11 ± 5.78 | 0.12 | 0.76 | 0.99 |
| Sleep latency (min) | 10.63 ± 9.59 | 25.59 ± 20.73 | 13.29 ± 10.48 | 18.77 ± 20.18 | 0.004 | 0.21 | 0.07 |
| REM latency (min) | 145.91 ± 60.43 | 154.24 ± 61.50 | 170.52 ± 69.38 | 148.34 ± 49.34 | 0.65 | 0.17 | 0.88 |
| REM (% TST) | 14.63 ± 6.76 | 15.93 ± 5.41 | 13.43 ± 5.41 | 17.39 ± 5.22 | 0.34 | 0.007 | 0.12 |
| Stage 1 (% TST) | 2.22 ± 1.98 | 4.26 ± 4.88 | 2.23 ± 1.72 | 2.81 ± 3.65 | 0.07 | 0.45 | 0.47 |
| Stage 2 (% TST) | 30.56 ± 12.27 | 36.46 ± 11.77 | 26.95 ± 12.16 | 38.42 ± 11.04 | 0.10 | 0.001 | 0.02 |
| Stages 1 and 2 (% TST) | 32.78 ± 13.15 | 40.72 ± 14.25 | 29.18 ± 12.8 | 41.23 ± 12.57 | 0.10 | 0.001 | 0.02 |
| Slow wave sleep (% TST) | 52.59 ± 14.11 | 43.35 ± 13.16 | 57.48 ± 11.41 | 41.38 ± 11.73 | 0.03 | <0.001 | <0.001 |
| Nadir $SpO_2$ over 10 s (%) | 90.04 ± 3.30 | 90.30 ± 4.23 | 91.32 ± 3.73 | 89.07 ± 4.88 | 0.82 | 0.06 | 0.40 |
| Time $SpO_2 < 90\%$ (min) | 0.88 ± 1.75 | 0.97 ± 2.22 | 0.15 ± 0.30 | 0.87 ± 1.96 | 0.89 | 0.07 | 0.98 |
| Total arousal index (events/h TST) | 13.55 ± 6.22 | 12.60 ± 6.97 | 15.48 ± 7.57 | 12.70 ± 7.81 | 0.63 | 0.18 | 0.67 |
| Respiratory arousal index (events/h TST) | 1.67 ± 2.25 | 2.44 ± 3.49 | 3.22 ± 2.94 | 5.14 ± 4.00 | 0.38 | 0.04 | <0.001 |
| LMI (events/h TST) | 3.40 ± 2.93 | 5.12 ± 2.69 | 2.77 ± 3.40 | 4.84 ± 2.44 | 0.04 | 0.01 | 0.07 |
| PLMI (events/h TST) | 0.71 ± 1.90 | 2.03 ± 4.35 | 0.97 ± 2.90 | 1.93 ± 3.82 | 0.19 | 0.30 | 0.15 |
| RRLMI (events/h TST) | 0.03 ± 0.09 | 0.18 ± 0.38 | 0.18 ± 0.51 | 0.36 ± 0.48 | 0.06 | 0.17 | 0.001 |

AHI, apnea–hypopnea index; TST, total sleep time; REM, rapid eye movement; REM (% TST), the ratio of REM to TST; stage 1 (% TST), the ratio of stage 1 to TST; stage 2 (% TST), the ratio of stage 2 to TST; slow wave sleep (% TST), the ratio of slow wave sleep to TST; nadir $SpO_2$, the lowest $O_2$ saturation associated with a respiratory event; time $SpO_2 < 90\%$, the period of $SaO_2 < 90\%$; LMI, leg movement index; PLMI, periodic leg movement index; RRLMI, leg movement index related respiratory event.
Data are presented as mean ± standard deviation.
[a] Non-asthmatic children in AHI ≤ 5 group.
[b] Asthmatic children in AHI ≤ 5 group.
[c] Non-asthmatic children in AHI > 5 group.
[d] Asthmatic children in AHI > 5 group.

Third, asthmatic children both with or without moderate to severe obstructive sleep apnea had significantly more leg movement than AHI-range-matched BMI-range-matched non-asthmatic children. According to the findings of this study, PSG supports the hypothesis that non-obese asthmatic children, with or without moderate to severe obstructive sleep apnea, will exhibit poor sleep quality as compared with non-obese non-asthmatic children.

Obstructive sleep apnea might suffer from increasing nasal resistance such as nasal mucosa edema among asthmatic subjects [23]. Furthermore, obesity and sleep apnea have been confounding factors in the objective sleep study of asthmatic children and non-asthmatic children in the past [7]. To clarify the confounding effects of asthma and obstructive sleep apnea, this study was designed to exclude obesity and stratify the results for with or without moderate to severe obstructive sleep apnea and with or without asthma into four groups. The cutoff point for the apnea–hypopnea index over 5 events per hour during sleep was considered as a pathological breathing problem [24]. In previous research, Kaditis et al. founded that children with history of wheezing had significantly more frequently tonsillar hypertrophy than those without wheezing [25]. In our study, the snore index in asthmatic children with AHI > 5/h was showed significant higher than those in non-asthmatic children with AHI ≤ 5/h. Tonsillar hypertrophy maybe mediates the association between asthma and obstructive sleep-disordered breathing among children.

In this study, asthmatic children without moderate to severe obstructive sleep apnea took a longer time to fall asleep compared with non-asthmatic children without moderate to severe obstructive sleep apnea. Previous study found that the sleep latency in asthmatic children was significantly longer compared with non-asthmatic children [17]. Further research is therefore required to clarify whether longer sleep latency among asthmatic children will debilitate health conditions.

Slow-wave sleep has been demonstrated to play an important role in strengthening memory [26], which might have an impact on learning during childhood. Peigneux et al. [27] found that humans process memory traces during slow wave sleep. Slow wave sleep was found to be reduced in insomniac subjects compared with healthy subjects, and a reduction in slow wave sleep was significantly associated with reduced memory [28]. In our study, asthmatic children had significantly less slow wave sleep than non-asthmatic children in either the sleep apnea group or the non-sleep apnea group. In addition, asthmatic children with moderate to severe obstructive sleep apnea had longer NREM stage 1 and 2 and REM sleep compared with non-asthmatic children with moderate to severe obstructive sleep apnea. Reduction in slow wave sleep has been reported in children with asthma in a previous study [29]. Because childhood is an important period for brain maturity, the impact of slow wave sleep might have a more severe outcome than in older children. The association of a decrease in slow wave sleep and memory among asthmatic children will need further investigation.

Restless leg syndrome during sleep in children is associated with pathologic conditions such as asthma [30]. Leg jerking and kicking were observed during sleep in some children [31]. In this study, there were more movement events of the anterior tibialis muscles in asthmatic children with or without moderate to severe obstructive sleep apnea. Children with wheezing (a symptom of asthma) had a higher risk of restless sleep compared to children without wheezing [32,33]. The observed symptom of leg jerking and kicking needs to be evaluated for clinical presentations during sleep in children. In addition, asthmatic children with AHI > 5 had significant higher snore index, respiratory arousal index, and RRLMI to non-asthmatic children with AHI ≤ 5/h. It is still unknown whether restless leg movements may cause poor sleep quality. Therefore, the impact of leg movement on sleep also needs further investigation.

The CBCL has been found to be a good instrument for assessing the emotional and behavioral problems of children and adolescents [34]. Our result shows that asthmatic children had no greater level of behavioral problems than non-asthmatic children with and without moderate to severe obstructive sleep apnea. In previous studies, asthmatic children with average severity in moderate level (range from mild to severe) had significantly higher scores on internalizing, externalizing, and total problem scores compared with non-asthmatic children [35,36]. However, CBCL total problem score was associated with the severity and the duration of illness [35]. Our findings are not in accordance with these previous studies. The reason for this may be that the severity of asthma in our subjects is at a relatively mild level. These emotional and behavioral findings did not support our hypothesis that asthmatic children will exhibit a poorer grade in behavioral problems, compared with non-obese AHI-range-matched BMI-range-matched non-asthmatic children.

There are some limitations in this study. First, the severity of the disease was diagnosed as mild asthma by pediatricians, and two subjects were regularly taking asthma medicine (Singulair, montelukast sodium) while others did not take any medication. Asthmatic conditions might get worse with increasing severity of sleep quality [37]. Secondly, we did not execute the diagnosis of allergic rhinitis for children by clinical test. The probability of allergic rhinitis in asthmatic children is higher than non-asthmatic children according to parent reports. It might have unknown co-effects on sleep between asthma and allergic rhinitis. Third, because we excluded the confounding factor obesity, the current findings were only suitable for non-obese asthma and SDB cases [7]. Fourth, children without any apnea or hypopnea (AHI < 1) were difficult to be recruited in the current study.

In summary, non-obese asthmatic children had sleep disturbances with less slow wave sleep relative to AHI-range-matched group. Besides, the effect of asthma plus sleep apnea appeared to have sleep disturbance in slow wave sleep, snore, respiratory arousal, and leg movement due to respiratory event. The findings of this study suggest that sleep conditions could be noticed and examined in children with asthma.

## Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.04.017.

## Acknowledgements

This work was supported by the grants from Asia University [102-asia-18] granted by Shu-Ping Lee, National Science Council Taiwan [NSC 100-2314-B-039 -016 -MY] granted by Hua Ting and by Taiwan Department of Health Clinical Trial and Research Center of Excellence [DOH102-TD-B-111-004]. We thank Dr. Tim Williams for his support throughout the editing process. Finally, we also gratefully acknowledge and thank the children and parents who participated in the study.

## References

[1] Kieckhefer GM, Lentz MJ. Nocturnal asthma in children. Adv Nurse Pract 2006;14:53–6.
[2] Meijer GG, Postma DS, Wempe JB, Gerritsen J, Knol K, van Aalderen WM. Frequency of nocturnal symptoms in asthmatic children attending a hospital out-patient clinic. Eur Respir J 1995;8:2076–80.
[3] American Thoracic Society. Standards and indications for cardiopulmonary sleep studies in children. Am J Respir Crit Care Med 1996;153:866–78.
[4] Malakasioti G, Gourgoulianis K, Chrousos G, Kaditis A. Interactions of obstructive sleep-disordered breathing with recurrent wheezing or asthma and their effects on sleep quality. Pediatr Pulmonol 2011;46:1047–54.

[5] Ng AK, Guan C. Impact of obstructive sleep apnea on sleep-wake stage ratio. Conf Proc IEEE Eng Med Biol Soc 2012;2012:4660–3.
[6] Eiseman NA, Westover MB, Ellenbogen JM, Bianchi MT. The impact of body posture and sleep stages on sleep apnea severity in adults. J Clin Sleep Med 2012;8:655–66A.
[7] Fiorino EK, Brooks LJ. Obesity and respiratory diseases in childhood. Clin Chest Med 2009;30:601–8.
[8] Chugh IM, Khanna P, Shah A. Nocturnal symptoms and sleep disturbances in clinically stable asthmatic children. Asian Pac J Allergy Immunol 2006;24:135–42.
[9] Fitzpatrick MF, Martin K, Fossey E, Shapiro CM, Elton RA, Douglas NJ. Snoring, asthma and sleep disturbance in Britain: a community-based survey. Eur Respir J 1993;6:531–5.
[10] Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman J Jr, et al. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. Sleep 2005;28:499–521.
[11] Ramagopal M, Scharf SM, Roberts DW, Blaisdell CJ. Obstructive sleep apnea and history of asthma in snoring children. Sleep Breath 2008;12:381–92.
[12] Ramagopal M, Mehta A, Roberts DW, Wolf JS, Taylor RJ, Mudd KE, et al. Asthma as a predictor of obstructive sleep apnea in urban African-American children. J Asthma 2009;46:895–9.
[13] Feitosa CA, Santos DN, Barreto do Carmo MB, Santos LM, Teles CA, Rodrigues LC, et al. Behavior problems and prevalence of asthma symptoms among Brazilian children. J Psychosom Res 2011;71:160–5.
[14] Wamboldt MZ, Fritz G, Mansell A, McQuaid EL, Klein RB. Relationship of asthma severity and psychological problems in children. J Am Acad Child Adolesc Psychiatry 1998;37:943–50.
[15] Fagnano M, van Wijngaarden E, Connolly HV, Carno MA, Forbes-Jones E, Halterman JS. Sleep-disordered breathing and behaviors of inner-city children with asthma. Pediatrics 2009;124:218–25.
[16] Stores G, Ellis AJ, Wiggs L, Crawford C, Thomson A. Sleep and psychological disturbance in nocturnal asthma. Arch Dis Child 1998;78:413–19.
[17] Jensen ME, Gibson PG, Collins CE, Hilton JM, Latham-Smith F, Wood LG. Increased sleep latency and reduced sleep duration in children with asthma. Sleep Breath 2013;17:281–7.
[18] Avital A, Godfrey S, Springer C. Exercise, methacholine, and adenosine 5′-monophosphate challenges in children with asthma: relation to severity of the disease. Pediatr Pulmonol 2000;30:207–14.
[19] Li AM, Au CT, Sung RY, Ho C, Ng PC, Fok TF, et al. Ambulatory blood pressure in children with obstructive sleep apnoea: a community based study. Thorax 2008;63:803–9.
[20] Chen W, Chang M-H. New growth charts for Taiwanese children and adolescents based on World Health Organization standards and health-related physical fitness. Pediatrics & Neonatology 2010;51:69–79.
[21] The Atlas Task Force. Recording and scoring leg movements. Sleep 1993;16:748–59.
[22] Yang HJ, Soong WT, Chiang CN, Chen WJ. Competence and behavioral/emotional problems among Taiwanese adolescents as reported by parents and teachers. J Am Acad Child Adolesc Psychiatry 2000;39:232–9.
[23] Alkhalil M, Schulman E, Getsy J. Obstructive sleep apnea syndrome and asthma: what are the links? J Clin Sleep Med 2009;5:71.
[24] Guilleminault C, Lee JH, Chan A. Pediatric obstructive sleep apnea syndrome. Arch Pediatr Adolesc Med 2005;159:775.
[25] Kaditis AG, Kalampouka E, Hatzinikolaou S, Lianou L, Papaefthimiou M, Gartagani-Panagiotopoulou P, et al. Associations of tonsillar hypertrophy and snoring with history of wheezing in childhood. Pediatr Pulmonol 2010;45:275–80.
[26] Born J. Slow-wave sleep and the consolidation of long-term memory. World J Biol Psychiatry 2010;11(Suppl. 1):16–21.
[27] Peigneux P, Laureys S, Fuchs S, Collette F, Perrin F, Reggers J, et al. Are spatial memories strengthened in the human hippocampus during slow wave sleep? Neuron 2004;44:535–45.
[28] Backhaus J, Junghanns K, Born J, Hohaus K, Faasch F, Hohagen F. Impaired declarative memory consolidation during sleep in patients with primary insomnia: influence of sleep architecture and nocturnal cortisol release. Biol Psychiatry 2006;60:1324–30.
[29] Kales A, Kales JD, Sly RM, Scharf MB, Tan T-L, Preston TA. Sleep patterns of asthmatic children: all-night electroencephalographic studies. J Allergy 1970;46:300–8.
[30] Martinez S, Guilleminault C. Periodic leg movements in prepubertal children with sleep disturbance. Dev Med Child Neurol 2004;46:765–70.
[31] Picchietti DL, Walters AS. Moderate to severe periodic limb movement disorder in childhood and adolescence. Sleep 1999;22:297–300.
[32] Verhulst SL, Vekemans K, Ho E, Aerts L, Jacobs S, De Backer LA, et al. Is wheezing associated with decreased sleep quality in Sri Lankan children? A questionnaire study. Pediatr Pulmonol 2007;42:579–83.
[33] Desager KN, Nelen V, Weyler JJ, De Backer WA. Sleep disturbance and daytime symptoms in wheezing school-aged children. J Sleep Res 2005;14:77–82.
[34] Cox KF. Investigating the impact of strength-based assessment on youth with emotional or behavioral disorders. J Child Fam Stud 2006;15:278–92.
[35] Eksi A, Molzan J, Savasir I, Guler N. Psychological adjustment of children with mild and moderately severe asthma. Eur Child Adolesc Psychiatry 1995;4:77–84.
[36] Park J, Kim BJ, Kwon JW, Song YH, Yu J, Kim HB, et al. Patterns of psychosocial adaptation and allergic disorders in Korean schoolchildren. Int Arch Allergy Immunol 2011;154:249–57.
[37] Yuksel H, Sogut A, Yilmaz O, Demet M, Ergin D, Kirmaz C. Evaluation of sleep quality and anxiety-depression parameters in asthmatic children and their mothers. Respir Med 2007;101:2550–4.